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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,721	07/11/2001	Bruce Acres	017753-132	7786

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EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	9

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,721	ACRES ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20,21 and 23-29* is/are pending in the application.

4a) Of the above claim(s) *11-17,20,23-25 and 27-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,18,21 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 April 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-10, 18, 21, and 26, in Paper No. 8 is acknowledged. The traversal is on the ground(s) that both Groups I and II are directed to a biological material (a nucleic acid and a target cell comprising the nucleic acid), and that it would not place an undue burden on the Examiner to examine both groups, thus, request rejoining of group II and I. This is not found persuasive because it is maintained that each of the Inventions requires a separate search status and consideration. A nucleic acid molecule or a genetically modified cell are structurally and functionally different materials and are separately classified. The different materials belong to different chemical entities, have distinct mode of operation, and require distinct considerations. The searches for groups II and I would have certain overlap, but they are not co-extensive. M.P.E.P. states, "FOR PURPOSES OF THE INITIAL REQUIREMENT, A SERIOUS BURDEN ON THE EXAMINER MAY BE PRIMA FACIE SHOWN IF THE EXAMINER SHOWS BY APPROPRIATE EXPLANATION OF SEPARATE CLASSIFICATION, OR SEPARATE STATUS IN THE ART, OR A DIFFERENT FIELD OF SEARCH AS DEFINED IN MPEP § 808.02". Therefore, it is maintained that these inventions are distinct due to their divergent subject matter. Further search of group II is not co-extensive, as indicated by the separate classifications. The requirement is still deemed proper and is therefore made **FINAL**.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the

Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 1-18, 20, 21, 23-29 are pending, however, claims 11-17, 20, 23-25, and 27-29 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1-10, 18, 21, and 26 are under current examination.

Specification

The abstract of the disclosure is objected to because this application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b).

Furthermore, it is noted that the abstract in WO 00/24896, the priority document for instant application, contains languages that should be avoided as indicated in MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

An abstract on a separate sheet is required.

Claim Objections

Claim 1 is objected to because of the following informalities: claim 1 encompasses more than one invention as defined in Paper #7, upon election of an invention for examination, said claim should be amended so that it only reads upon the elected invention. Thus, claim 1 will be examined to the extent that it reads on the elected invention.

Claim 6 is objected to because the meaning of the word "or" in line 2 of claim 6 is unclear in the context of the claim.

Claim 21 is objected to because of the following informalities: according to MPEP, each claim should begin with a capital letter, preferably an article such as "A", "The", etc. See MPEP § 608.01(m).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 18, 21, and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings, or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement;* Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

The claims are directed to a nucleic acid sequence containing at least one gene of therapeutic agent, and "elements which ensure the expression of said gene in vivo in target cells" (claim 1), wherein the nucleic acid further comprises "at least one DNA sequence which ensures the expression of a compound which is involved in the activation of cytotoxic effector cells or helper T lymphocytes" (claim 18). Given the broadest reasonable interpretation, the term "elements which ensure the expression of said gene in vivo in target cells", "DNA sequence which ensures the expression of a compound", and "a compound which is involved in the activation of cytotoxic effector cells or helper T lymphocytes" encompass numerous (genus) elements, DNA sequences, and compounds. However, the specification fails to define the terms of

elements, sequences, and compounds, even though a promoter/enhancer region would be included in the genus of elements, the claims embrace much more elements, thus, the specification fails to provide an adequate disclosure for the genus of the claimed invention in terms of distinguishing structural characteristics of the genus.

An adequate written description for an element, a DNA sequence, or a compound requires more than a mere statement that it is part of the invention; what is required is a description of the chemical structures and physical properties of the compound itself. It is not sufficient to define the agents solely by its principal biological property, i.e. "which ensure the expression of said gene in vivo in target cells", "which ensures the expression of a compound", and "which is involved in the activation of cytotoxic effector cells or helper T lymphocytes", because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any agent with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all agents that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). The court has made it very clear "CONCEPTION OF CHEMICAL COMPOUND REQUIRES THAT INVENTOR BE ABLE TO DEFINE COMPOUND SO AS TO DISTINGUISH IT FROM OTHER MATERIALS, AND TO DESCRIBE HOW TO OBTAIN IT, RATHER THAN SIMPLY DEFINING IT SOLELY BY ITS PRINCIPAL

BIOLOGICAL ACTIVITY". *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention

Claims 1-10, 18, 21, and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided.

Claim 21 recites a pharmaceutical composition of claim 1, and claim 1 clearly recites a biological material for teating mammals and any nucleic acid carrying any therapeutic gene of interest and elements that ensure the expression of said gene in any target cell *in vivo*. With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. "WHEN A COMPOUND OR COMPOSITION CLAIM IS LIMITED BY A

PARTICULAR USE, ENABLEMENT OF THAT CLAIM SHOULD BE EVALUATED BASED ON THAT USE". (MPEP 2164.01c) When analyzing the enabled scope of the claims, the intended use is to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. "A pharmaceutical composition" such as recited in the instant claims is defined as a composition for therapeutic use, to prevent, alleviate, treat, or cure a disease within the animal to which the substance is administered, therefore, will be evaluated by the standard. As such, the broadest reasonable interpretation of the claimed invention properly encompasses any gene therapy or vaccine composition, therefore, the claims will be evaluated by that standard.

In view of the guidance provided, the specification teaches generally to use the nucleic acids in gene therapy protocols (pages 14-17), the working examples teach construction of recombinant MVA viruses expressing antibodies recognizing T cell receptors, expressing such in the cell culture, and effects on the proliferation of murine splenocytes. However, the specification fails to teach the *in vivo* aspect of the invention, e.g. how to deliver the vectors so that they reach a significant numbers of target cells selectively, and whether a therapeutic effect could be achieved *in vivo*. Therefore, fails to provide an enabling disclosure to support the full scope of the invention.

While progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired cells *in vivo* continues to be unpredictable and inefficient as supported by numerous teachings available in the art. For example, *Deonarain* (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicates that one of the biggest problems hampering successful gene therapy is the "ABILITY TO TARGET A GENE TO A SIGNIFICANT

POPULATION OF CELLS AND EXPRESS IT AT ADEQUATE LEVELS FOR A LONG ENOUGH PERIOD OF TIME" (page 53, first paragraph). Deonarain reference gives high hope to targeted gene delivery, but the discussed strategies are still under investigation, and at the time, they were much less efficient than viral gene delivery (Conclusion), "GENE DELIVERY BY LIGAND TARGETED RECEPTOR-MEDIATED ENDOCYTOSIS OF POLYPLEXES *SHOULD* FIND ITS WAY INTO SOME MAIN LINE GENE THERAPY TREATMENT SCHEMES... HOWEVER, IN ORDER TO ACHIEVE THE LEVELS OF GENE TRANSFECTION AND EXPRESSION SEEN WITH RETROVIRAL VECTORS, FURTHER ADVANCES NEED TO BE MADE IN FIELDS SUCH AS MAMMALIAN ARTIFICIAL CHROMOSOMES" (paragraph bridging pages 65-66). Another dilemma for gene transfer is the rate of gene targeting. *Russell et al* (Nat Genet 1998 Apr; 18:325-30) review "IT IS CURRENTLY POSSIBLE TO INTRODUCE DEFINED MUTATIONS INTO MAMMALIAN CHROMOSOMES BY GENE TARGETING USING TRANSFECTION (ELECTROPORATION OR CALCIUM-PHOSPHATE PRECIPITATION) OR MICROINJECTION METHODS. TRANSFECTION TECHNIQUES USUALLY PRODUCE HOMOLOGOUS RECOMBINATION EVENTS IN ONLY A SMALL FRACTION OF THE TOTAL CELL POPULATION.(...) CHROMOSOMAL GENE-TARGETING EXPERIMENTS HAVE BEEN PERFORMED WITH RETROVIRAL AND ADENOVIRAL VECTORS, BUT THE RECOMBINATION RATES WERE NOT SIGNIFICANTLY HIGHER THAN THOSE OBTAINED BY TRANSFECTION. (2nd paragraph, page 325) *Boucher et al* (J Clin Invest 1999 Feb; 103:441-5) review that host cell resistance to foreign gene is another difficulty for successful in vivo gene transfer. "DESPITE AN IMPRESSIVE AMOUNT OF RESEARCH IN THIS AREA, THERE IS LITTLE EVIDENCE TO SUGGEST THAT AN EFFECTIVE GENE-TRANSFER APPROACH FOR THE TREATMENT OF CF LUNG DISEASE IS IMMINENT. THE INABILITY TO PRODUCE SUCH A THERAPY REFLECTS IN PART THE LEARNING CURVE WITH RESPECT TO VECTOR TECHNOLOGY AND THE FAILURE TO APPRECIATE THE CAPACITY OF THE AIRWAY EPITHELIAL CELLS TO DEFEND THEMSELVES AGAINST THE PENETRATION BY MOIETIES,

INCLUDING GENE-THERAPY VECTORS, FROM THE OUTSIDE WORLD". *Zink et al* (Gene Ther Mol Biol 2001 Jan;6:1-24) teach the reasons why the transgene would fail to achieve the expected effect in vivo, and indicated that in addition to the interaction of transcription factors with specific DNA elements, the transcription of mammalian genes and transgenes integrated into mammalian genomes is regulated at the levels of chromatin structure and nuclear architecture, "TRANSCRIPTIONAL REGULATION OF INTERGRATING GENE THERAPY VECTORS IS ONLY WELL INVESTIGATED AT THE MOLECULAR LEVEL, FEW DATA EXIST REGARDING THE INVOLVEMENT OF CHROMATIN STRUCTURE, AND VIRTUALLY NOTHING IS KNOWN ABOUT THE INVOLVEMENT OF NUCLEAR CHROMOSOME- AND GENOME ARCHITECTURE. THEREFORE, IT IS NOT SURPRISING THAT THE EXPRESSIONAL BEHAVIOR OF GENE THERAPY VECTORS AFTER INTEGRATION IS OFTEN UNPREDICTABLE AND DIFFICULT TO IMPROVE" (abstract).

The claims are drawn to using any naked polynucleotides and vectors. However, whether the recited vectors are suitable for the purpose of the instant invention are unclear. For example, retroviral vectors are known for their inability to infect non-dividing cells, which would be a critical limitation to the practice of the instant invention by *in vivo* gene therapy method. *Miller et al* (1995, FASEB J., Vol. 9, pages 190-199), acknowledge various vector system available in the art, then teach, "NO SINGLE DELIVERY SYSTEM IS LIKELY TO BE UNIVERSALLY APPROPRIATE, FOR INSTANCE, THE REQUIREMENTS OF GENE THERAPY FOR CYSTIC FIBROSIS ARE GREATLY DIFFERENT FROM THOSE OF CANCER" (1st paragraph, page 190). "ONCE AGAIN, TARGETING AT THE LEVEL OF THE VECTOR HAS NOT YET BEEN PARTICULARLY WELL DEVELOPED" (1st paragraph, page 198) *Makrides et al* (Protein Exp Pur 1999;17:183-202) teach "THE CHOICE OF AN EXPRESSION SYSTEM FOR PRODUCTION OF RECOMBINANT PROTEINS DEPENDS ON MANY FACTORS, INCLUDING CELL GROWTH CHARACTERISTICS,

EXPRESSION LEVELS, INTRACELLULAR AND EXTRACELLULAR EXPRESSION, POSTTRANSLATIONAL MODIFICATIONS AND BIOLOGICAL ACTIVITY OF THE PROTEIN OF INTEREST, AS WELL AS REGULATORY ISSUES AND ECONOMIC CONSIDERATIONS IN THE PRODUCTION OF THERAPEUTIC PROTEINS."

Thus, it is evident that at the time of the invention, the gene therapy practitioner, while acknowledging the significant potential of gene therapy, still recognized that such therapy was neither routine nor accepted, and awaited significant development and guidance for its practice. Therefore, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for such therapeutic regimen. Although the instant specification provides a brief review of a potential therapeutic use of the claimed vector and data from ex vivo studies, it is not enabled for its full scope because the specification does not disclose whether the nucleic acids encompassed by the claims would function properly in vivo, any significant gene transfer in any target cells *in vivo*, or any therapeutic effects *in vivo*. In summary, the teachings and guidance present in the specification, as a whole, represent an initial investigation into the feasibility of the development of a useful means for executing gene therapy that awaits further development to the practical level to be used as an in vivo pharmaceutical composition.

Accordingly, in view of the quantity of experimentation necessary to determine the parameters for achieving *in vivo* gene expression in selected target cells at therapeutic levels, in particular for the treatment of any and all diseases, the lack of direction or guidance provided by the specification as well as the absence of working examples with regard to a pharmaceutical composition used for *in vivo* gene therapy, and the breadth of the claims directed to the use of numerous therapeutic

genes/vectors/expression elements combinations, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 18, 21 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite because of claim recitation, "elements which ensure the expression of said gene in vivo in target cells" (claim 1), wherein the nucleic acid further comprises "at least one DNA sequence which ensures the expression of a compound which is involved in the activation of cytotoxic effector cells or helper T lymphocytes. The specification fails to define the term, it is unclear what the phrases embrace or exclude, and thus, the metes and bounds of the claims are unclear.

Claim 6 is vague and indefinite because of the claim recitation, "said vector comprises at least one said nucleic acid sequence", wherein the previous claim, from which it depends on, recites "said nucleic acid is a vector", the recitations are circular, it is unclear what applicants intend to claim, the metes and bounds of the claims are unclear. Claim 6 further recites "said vector comprises at least one said nucleic acid sequence complexed with a(?) substance" of a polymer group, it seems that a vector could comprise a nucleic acid but not a polymer substance.

Claims 1, 7, 8 are vague and indefinite because multiple phrases recite in the sentence, however, the interrelations of these phrases are unclear. For example, it is

unclear which cell "such a cell" refers to, and which is involved in the process of activation of such a cell, a T lymphocyte or a polypeptide? Thus, the metes and bounds of the claims are unclear.

Claim 18 is vague and indefinite because of the term "compound". A compound is defined as "something formed by a union of elements or parts; especially: a distinct substance formed by chemical union of two or more ingredients in definite proportion by weight" in a standard English dictionary, which embrace broad ranges of molecules, such as organic chemicals, whereas a DNA sequence could only express a polypeptide or a protein. The metes and bounds of the claim are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-4, 6-10, 18, 21, and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by *Schneck et al* (US 6,448,071).

Schneck et al teach a nucleic acid sequence encoding MHC class II or TCR heterodimers and murine antibody heavy and light chains in a baculaovirus expression system (therapeutic gene of interest, abstract), wherein the expressed fusion product has high affinity to CTL (capable of binding a polypeptide at the surface of a CTL, 2C T cell, examples 3-5), wherein the expression system comprises promoters and enhancers that would ensure the expression of said gene of interest *in vivo* in a target cell (column 13), wherein said nucleic acid sequence could be in the form of a naked polynucleotide or a vector (column 15, line 15), wherein the vector could be complexed with a cationic polymer (column 15, lines, 37-55), wherein the heavy or light chain of the antibody is fused with a transmembrane polypeptide (claims 1 & 9, and column 5, lines 40-41), wherein the transmembrane polypeptide is a glycoprotein TCR α/β chain (claim 12, column 2, line 15), which is on the membrane of CD4+ T cell (column 2, lines 63-65), thus, the teaching meets limitation of instant claim 7. A promoter would ensure the expression of MHC/TCR (compound involved in the activation of CTL or Th lymphocytes), thus, the limitation of instant claim 18 is also met. *Schneck et al* teach a composition comprises said polynucleotide and a copolymer such as polyethylene glycol (column 15, lines 37-55). Therefore, *Schneck et al* anticipate the instant claims.

Please note that the claim recitation "for treating mammals" has not been given patentable weight in this rejection and the following rejection. This is because it merely recites an intended use of the biological material, wherein there is no structural or manipulative difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a

process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claims 1-6, 18, 21, and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by *Wang et al* (US 6,132,980).

Wang et al teach a nucleic acid construct encoding a therapeutic gene of interest, i.e. a tumor antigen that could be recognized by CTL (column 11, lines 26-34), wherein the construct could be a naked DNA (column 8, line 1) or a recombinant viral vector such as MVA (column 11, line 47), wherein the expression system comprises promoters and enhancers that would ensure the expression of said gene of interest *in vivo* in a target cell and the expression of the tumor antigen, which is involved in the activation of CTL against tumor cells, thus, the limitation of instant claim 18 is met. *Wang et al* teach that the polynucleotide could co-transfected with a cationic lipid (column 12, lines 7-16). Therefore, *Wang et al* anticipate the instant claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
November 21, 2002

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER